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REMARKS

Claims 14-20 and 25-31 are pending in this application, and no claim has been allowed.

Formal Matters

Applicants acknowledge the withdrawal of the finality of the previous Action and the entry of the request for continued examination.

Applicants also gratefully acknowledge the entry of the amendment and response filed August 7, 2003 (Paper No. 10).

Applicants acknowledge the withdrawal of the outstanding rejection of claims 14, 15, 17, 19, 20, and 25-27 under 35 U.S.C. § 102 (e) as allegedly being anticipated by Burmer, U.S. Patent No. 6,087,103 and the withdrawal of the outstanding rejection of claims 16, 18, and 28-31 under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Burmer in view of Baek or Verma and in view of Kutsuna.

Rejections under 35 U.S.C. § 103 (a)

Claims 14-15, 17, 19-20 and 25-27 are rejected under 35 U.S.C. §103 (a) as allegedly unpatentable over Burmer (U.S. Patent No. 6,087,103) in view of Upadhyay *et al.* (U.S. Patent No. 5,962,515). The Action acknowledges that Burmer lacks disclosure of extracting and fractionating compounds from crude plant using chromatography. The Examiner asserts that Upadhyay discloses the fractionating and purifying of a crude plant extract and teaches that compounds are conventionally extracted and purified from plant sources for use in drug discovery screening assays. Thus, according to the Examiner, it would have been obvious to extract and fractionate compounds from crude plant as taught by Upadhyay in a screening system as taught by Burmer. Claims 16, 29 and 30 are rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Burmer in view of Upadhyay *et al.* and further in view of Baek *et al.* (*Agricultural Chemistry and Biotechnology*, April 1998 (Abstract)) or Verma *et al.* (*Journal of*

Medicinal and Aromatic Plant Sciences, September 1997). According to the Examiner, Baek and Verma each teach the extracting and fractionating of compounds from *Carthamus tinctorius* and Verma disclose that these biologically active compounds have antithrombotic capacity. Claims 18 and 28 are rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Burmer in view of Upadhyay *et al.* and further in view of Kutsuna *et al.* (*Journal of the Pharmaceutical Society of Japan* (November 1988) (Abstract)). According to the Examiner, Kutsuna discloses the isolation, identification, and the determination of a biologically active compound from *C. tinctorius* that is a platelet aggregation inhibitor which exhibits in vivo anti-thrombotic activity, which inhibits glycoprotein (GPIIbIIIa) binding to serum proteins, induced by adenosine diphosphate, and is identified as adenosine. Claim 31 is rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Burmer in view of Upadhyay *et al.* and further in view of Baek or Verma and further in view of Kutsuna. According to the Examiner, Kutsuna discloses a compound identified as adenosine that has the inherent properties of a molecular weight of 268 gm/mole and is self-polymerizable. Applicants traverse these rejections.

Applicants respectfully submit that Burmer and Upadhyay in combination with any of the cited references fails to teach or suggest every element of the invention of the instant methods, and therefore none of the cited combinations result in the claimed methods, failing to render these methods *prima facie* obvious.

As a preliminary matter, each combination of references relies on the teachings of Burmer regarding the selective binding of compounds to target proteins. Applicants again submit that Burmer fails to teach or suggest the method of selection of the claimed methods, and thus its combination with any or all of the cited references fails to render the claimed methods *prima facie* obvious. A thorough review of Burmer reveals the distinct, and non-obvious, nature of the instant methods. According to the Examiner, the compounds selectively bind to a target protein, citing column 8, lines 12-65 and column 15, lines 8-24 of Burmer. *See* Paper No. 15, at page 4. Column 8, lines 12-65 discloses general recombinant nucleic acid methods and methods of isolating nucleic acids. More specifically, this section of the patent discloses the isolation of nucleic acids sequences and the making of cDNA libraries. There is no disclosure regarding the use of protein libraries extracted from any source including plants. Column 15, lines 8-24 discloses kits. This cited section

also lacks any disclosure regarding proteins, or more specifically plant protein extracts. To date, the Examiner has not provided a single citation within Burmer that teaches or suggests the use of proteins extracted from plants as the immobilized target in the a selection assay. The Examiner then alleges that the "compounds [of Burmer] are each incorporated into a different location (ligand address) that corresponds to a tag having a known address identified by reference to a matrix on a solid support (a well on a microtiter plate) and a corresponding location on a membrane (plastic microtiter plate)", citing column 11, lines 16-64. Applicants note that at the citation provided by the Examiner, Burmer states:

> The individual components of the tag, ligand, and target libraries are each provided with an address. ... The purpose of the substrate is to use spatial positioning of an array (e.g., of targets) to allow identification of the individual target polypeptides.

See Burmer, at column 11, lines 16-17 and 21-23 (emphasis added). The claimed methods do not position individual components of the libraries on a substrate that allows immediate identification of individual target polypeptides. Instead, the claimed method position individual fractions of plant extracts on substrate. Each of these fractions contains multiple different components that share a similar molecular weight and charge. Based on the positioning of the plant extracts on the substrate, it is **impossible** to identify individual target polypeptides. In other words, after a selection using Burmer's methods, one can immediately identify both the target and the ligand bound to the target. In contrast, the instant methods do not permit such identification. Therefore, the purpose of Burmer cannot be achieved using the claimed methods. *See* MPEP § 2143.01 ("If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." (citations omitted)).

Upadhyay fails to remedy the deficiencies in Burmer. First, Upadhyay fails to provide any teaching or suggestion to modify the teachings of Burmer so that both the target and ligand cannot be immediately identified. Second, Upadhyay's disclosure regarding fractionation actually teaches away from the claimed methods. Upadhyay uses repeated extractions under very specific conditions to identify compounds active in biological assays from a single plant, *Piper longum*. Upadhyay fails to teach or suggest that such methods would be suitable for other plants. In fact, Upadhyay is completely silent with regards to any plant other than *Piper longum*. Therefore, the

combination of Burmer and Upadhyay fail to result in the claimed methods.

The further addition of Baek, Verma, and Kutsuna do not remedy the deficiency in Burma. Baek and Kutsuna rely on a single extraction step to isolate compounds. Baek has no teaching regarding additional steps after the fractionation useful in identifying compounds. Kutsuna teaches only the use of nuclear magnetic resonance to identify compounds following fractionation of plant extracts. Verma reviews the chemistry and biology of *Carthamus tinctoris*. Verma has no teaching or suggestion as to how to identify compounds in *Carthamus tinctoris* or, for that matter, other plants. In sum, neither Baek, Verma, nor Kutsuna teach or suggest the use of target-binding properties to identify compounds in plant extracts. Therefore, the combination of Burmer and Upadhyay with Baek or Verma in view of Kutsuna fails to result in the claimed methods. As a case of *prima facie* obviousness requires that the combined references result in the claimed methods, the absence of such teachings renders the claimed methods nonobvious.

Applicants submit that there is no motivation or suggestion to combine these references to use a single labeled target (or tagged ligand) to identify compounds in immobilized plant extracts. "There must be some suggestion for [combining prior art references] found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." *In re Jones,* 21 U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992). Burmer does not suggest the use of plant extracts. Upadhyay teaches the use of very specific extraction methods for a particular plant. The success of using extraction alone actually *teaches away* from a need to employ any additional methods to identify such compounds. Both Baek and Kutsuna lack any suggestion that modification of the disclosed methods are required to identify compounds, while Verma lacks any suggestion whatsoever regarding the identification of such compounds. In fact, the successful identification of some compounds using the methods of Upadhyay, Baek, or Kutsuna *teaches away* from the need to use any additional steps to identify such compounds. Hence, the combination of these references is improper and does not support the obviousness rejection.

Finally, the identification of compounds using the teachings of the combined references provides no reasonable expectation of success to the skilled artisan. High throughput screening of plant extracts differs in technologically meaningful ways from screening of purified protein or nucleotide libraries of, *e.g.*, Burmer. Natural product extracts typically are colored, insoluble, and

consists of numerous products that may interact (either synergistically or antagonistically), result in false positives, and present significant challenges in assay sensitivity which are not addressed by any of the references. To date, the Examiner has provided no rationale or objective reasoning why such difficulties are not relevant to the obviousness analysis while these same difficulties are acknowledged by those of skill in the art. *See* Clark, A., *Natural Products*, in FOYE'S PRINCIPLES OF MEDICINAL CHEMISTRY, 24, 29 (Williams, D.A., et al., eds., 5th Ed 2002) (already of record). Therefore, a method screening purified libraries does not provide any expectation of success for a method screening natural product extracts.

In light of the above, Applicants respectfully submit that the rejections under 35 U.S.C. § 103 (a) have been overcome. Therefore, the basis for this rejection may be withdrawn.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 205032000400. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 23, 2004

Respectfully submitted,

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